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Renal venous Doppler ultrasound – a new parameter for predicting outcomes in patients with decompensated heart failure

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ABSTRACT

Aim. To assess the frequency, dynamics, and prognostic value of renal venous congestion using Doppler ultrasound in patients with decompensated heart failure (DHF).

Materials and methods. A prospective, single-center study included 124 patients with DHF (mean age 70 ± 12 years, 51.6% were males), left ventricular ejection fraction (LVEF) 44 [34; 55] %, N-terminal pro B-type natriuretic peptide (NT-proBNP) 1,609 [591; 2,700] pg / ml. All patients underwent a standard physical examination and laboratory and instrumental tests, including the assessment of the NT-proBNP level. Renal venous blood flow was assessed using pulsed-wave Doppler ultrasound. The presence of continuous renal blood flow was considered as the absence of venous congestion, while intermittent blood flow (two-phase and single-phase flow) indicated venous congestion. Rehospitalization for DHF and reaching a composite endpoint (rehospitalization for DHF and cardiovascular mortality) within 12 months after discharge were selected as endpoints.

Results. At admission, continuous renal venous blood flow was observed in 34 (27.4%) patients, intermittent renal venous blood flow was found in 90 (72.6%) patients: two-phase flow in 62 (50%) and single-phase flow in 28 (22.6%) patients with DHF. At discharge, 66 (53.2%) patients had intermittent renal venous blood flow: two-phase flow in 50 (40.3%) and single-phase flow in 16 (12.9%) patients. Correlations of renal venous congestion with the levels of NT-proBNP, serum iron, uric acid, creatinine, LVEF, systolic pressure in the pulmonary artery (SPPA), and the development of acute kidney injury (AKI) were revealed. Persistent renal venous congestion at discharge was significantly associated with a higher probability of rehospitalization for DHF (hazard ratio (HR) 1.93 95% confidence interval (CI) (1.017–3.67); $p = 0.044$) and a composite endpoint (HR 2.66, 95% CI (1.43–4.96); $p = 0.002$).

Conclusion. In patients with DHF, it is necessary to evaluate renal venous blood flow using pulsed-wave Doppler ultrasound to stratify patients with development of cardiovascular complications within 12 months.

Keywords: DHF, renal venous blood flow, renal venous congestion, NT-proBNP

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Почечная венозная допплерография – новый параметр для прогнозирования исходов у пациентов с декомпенсацией хронической сердечной недостаточности

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РЕЗЮМЕ

Цель: оценить частоту, динамику и прогностическое значение почечного венозного застоя, оцененного с помощью допплерографии, у пациентов с декомпенсацией хронической сердечной недостаточности (ДХСН).

Материалы и методы. В проспективное одноцентровое исследование были включены 124 пациента с ДХСН, в том числе 51,6% мужчин, средний возраст 70 ± 12 лет. Пациенты имели следующие показатели: фракция выброса левого желудочка (ФВ ЛЖ) 44 [34;55]%, N-терминальный мозговой натрийуретический пептид (NT-proBNP1609) [591;2 700] пг/мл. Всем пациентам проводили стандартное физическое, лабораторно-инструментальные исследования, включая уровень NT-proBNP. Оценку почечного венозного кровотока проводили с помощью импульсно-волновой допплерографии. Наличие непрерывного почечного кровотока расценивали как отсутствие венозного застоя, в то время как прерывистый (двухфазный и однофазный кровоток) указывал на венозный застой. В качестве конечных точек были выбраны повторная госпитализация по поводу ДХСН и достижение комбинированной точки (регоспитализация по поводу ДХСН и сердечно-сосудистая смертность) в течение 12 мес после выписки.

Результаты. При поступлении непрерывный почечный венозный кровоток отмечался у 34 (27,4%), прерывистый почечный венозный кровоток – у 90 (72,6%): двухфазный – у 62 (50%) и однофазный – у 28 (22,6%) пациентов с ДХСН. При выписке у 66 (53,2%) пациентов сохранялся прерывистый почечный венозный кровоток: двухфазный – у 50 (40,3%) и однофазный – у 16 (12,9%). Выявлены корреляции почечного венозного застоя с уровнем NT-proBNP, сывороточного железа, мочевой кислоты, креатинина, ФВ ЛЖ, систолического давления в легочной артерии и развитием острого почечного повреждения. Сохраняющийся почечный венозный застой при выписке достоверно ассоциировался с более высокой вероятностью повторной госпитализации по поводу ДХСН (отношение рисков (ОР) 1,93 95%-й доверительный интервал (ДИ) (1,017–3,67); $p = 0{,}044$) и комбинированной конечной точки (ОР 2,66 95%-й ДИ (1,43–4,96); $p = 0{,}002$).

Заключение. У пациентов с ДХСН целесообразно оценивать почечный венозный кровоток с помощью импульсно-волновой допплерографии для стратификации пациентов с развитием сердечно-сосудистых осложнений в течение 12 мес.

Ключевые слова: ДХСН, почечный венозный кровоток, почечный венозный застой, NT-proBNP

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Соответствие принципам этики. Все пациенты подписали информированное согласие на участие в исследовании. Исследования одобрено локальным этическим комитетом РУДН (протокол № б/н от 16.11.2021).

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INTRODUCTION

In recent years, cardiorenal interactions in patients with decompensated heart failure (DHF) have attracted increasing attention due to a significant increase in the prevalence of combined cardiac and renal dysfunction. The frequency of deterioration in the functional state of the kidneys in patients with DHF is 45–63.6%, and it is an unfavorable prognostic factor leading to repeated hospitalizations and an increase in the cardiovascular mortality [1].

Currently, the role of venous congestion and an increase in central venous pressure in the deterioration of kidney function in DHF is being discussed [2]. Until recently, the diagnosis of renal venous congestion presented certain difficulties due to the invasiveness and laboriousness of the study.

N. Iida. et al. were the first to propose a method for assessing renal venous blood flow using Doppler ultrasound. P. Nijst et al. revealed the relationship between changes in the nature of renal venous blood flow using this technique and deterioration in kidney function in patients with DHF and recommended it to control diuretic therapy in patients with DHF [3, 4].

Currently, there are no universal criteria for detecting renal venous congestion, which emphasizes the relevance of studies to compare the clinical and prognostic value of the proposed method in patients with DHF.

The aim of the study was to assess the frequency, dynamics, and prognostic value of renal venous congestion in patients with DHF using Doppler ultrasound.

MATERIALS AND METHODS

A prospective, single-center study included 124 patients hospitalized at the Heart Failure Center of at Vinogradov City Clinical Hospital from December 2020 to December 2021 (Table 1). Exclusion criteria were malignant neoplasms in the active phase, severe valvular defects, and somatic symptom disorders.

All patients underwent standard clinical and laboratory tests, including determination of N-terminal pro-brain natriuretic peptide (NT–proBNP) (Vector-Best, Russia). The Stagnation Scale was used to assess clinical stagnation [5]. An ultrasound examination of the heart and renal blood flow was performed using the VIVID E90 premium system (GE, Healthcare).

The nature of the renal blood flow was assessed using pulsed-wave Doppler ultrasound with the patient lying on the left side using a convex or sector sensor with simultaneous ECG recording on the monitor of the device. Normally, the Doppler renal blood flow curve is continuous. A discontinuous renal blood flow pattern with systolic and diastolic phases (as a minor deviation) and a discontinuous flow pattern with a diastolic phase (as a pronounced deviation) were considered as venous congestion (Fig. 1) [6].

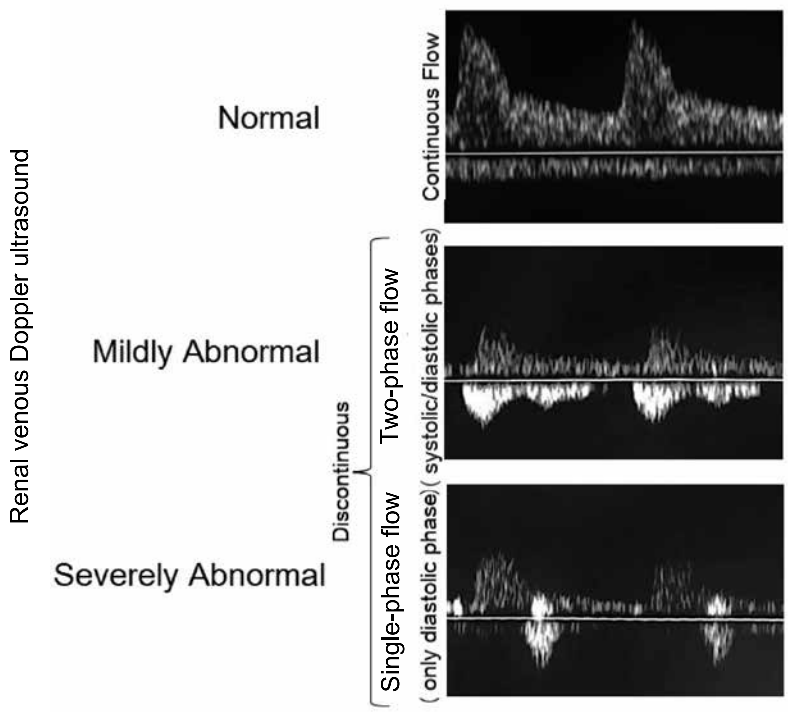

Fig. 1. Algorithm for the ultrasound assessment of renal venous blood flow

Table 1

Characteristics of patients with DHF, n = 124	
Parameter	Value
Gender, men, *n* (%)	64 (52)
Age, years, *M* ± *SD*	70 ± 12
BMI, kg / m², *Me [IQR]*	32.4 [27.7; 38.35]
Smoking, *n* (%)	23 (19)
Arterial hypertension, *n* (%)	110 (89)
Ischemic heart disease, *n* (%)	65 (52)
Atrial fibrillation, *n* (%)	73 (59)
Type 2 diabetes mellitus, *n* (%)	43 (35)
CKD, *n* (%)	91 (73.4)
AKI, *n* (%)	29 (23.4)
NYHA, FC, *n* (%) II III IV	 28 (22) 54 (44) 42 (34)
Stagnation Scale, score, *Me [IQR]*	9 [6; 12.5]
LVEF, %, *Me [IQR]*	44 [34; 55]
LVEF: < 40%, *n* (%) 41–49%, *n* (%) ≥ 50%, *n* (%)	 48 (38.7) 23 (18.5) 53 (42.8)
SPPA, mm Hg, *Me [IQR]*	48 [34; 60]
Renal venous blood flow pattern: continuous, *n* (%) discontinuous, *n* (%) two-phase, *n* (%) single-phase, *n* (%)	 34 (27.4) 90 (72.6) 62 (50) 28 (22.6)
NT-proBNP, pg / ml, *Me [IQR]*	1,609 [591; 2,700]
Creatinine, µmol / l, *Me [IQR]*	103.5 [84; 125]
GFR, ml / min / 1.73 m², *Me [IQR]*	54.3 [43; 67.4]
Blood potassium, mmol / l, *Me [IQR]*	4.35 [3.9; 4.6]
Urea, mmol / l, *Me [IQR]*	7.4 [5.3; 9.7]
Uric acid, mmol / l, *Me [IQR]*	438 [327; 570]
Iron, mmol / l, *Me [IQR]*	6.9 [4.4; 12.1]

Note: BMI – body mass index, AKI – acute kidney injury, SPPA – systolic pressure of the pulmonary artery, GFR – glomerular filtration rate, LVEF – left ventricular ejection fraction, FC HF – functional class of heart failure, CKD – chronic kidney disease, NT -proBNP – N-terminal brain natriuretic peptide (here and in Table 2–4).

All patients received standard HF therapy during and after hospitalization. The duration of follow-up after discharge was 12 months. The assessment of short-term and long-term outcomes was performed using the EMIAS database. Rehospitalization for DHF and death from cardiovascular complications during the follow-up period were selected as endpoints.

Statistical analysis was performed using Statistica (version 10.0; Statsoft), MedCalc Software's VAT Version 19.0, and SPSS (version 26.0). Quantitative data were presented as the arithmetic mean and the standard deviation of the mean *M* ± *SD* (for normal distribution) or as the median and the interquartile range *Me [IQR]* (for non-normal distribution). The significance of differences between the two groups of quantitative variables was assessed using the Mann – Whitney *U*-test and the Kruskal – Wallis test. Qualitative variables were represented by absolute and relative values *n* (%). To compare the groups by the frequency of qualitative variables, the Pearson's chi-square test ($\chi 2$) was used. The survival probability was estimated by constructing Kaplan – Meier survival curves; comparison was made using the log rank test. Univariate and multivariate Cox regression analysis models were used to assess the predictive value of different methods for the risk of death from or rehospitalization for DHF. The differences were considered statistically significant at $p < 0.05$.

RESULTS

On admission, the incidence of renal venous congestion in patients with DHF was 72.6%; at discharge, renal venous congestion persisted in 53.2% of patients. The dynamics of renal venous blood flow during hospitalization is shown in Fig. 2.

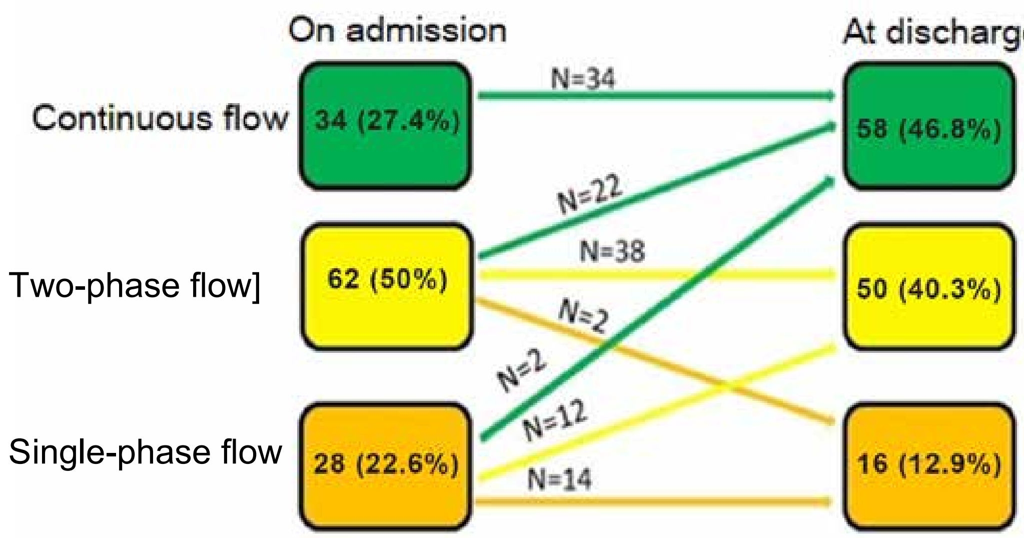

Fig. 2. Dynamics of renal venous blood flow

At admission, patients with renal venous congestion had significantly higher incidence of CKD in history, development of AKI during hospitalization, higher levels of SPPA, NT-proBNP, and uric acid, and lower serum iron levels compared to patients without renal venous congestion (Table 2). Table 3 shows comparative characteristics of patients with changes in renal venous blood flow at discharge. Associations of renal venous congestion on admission and discharge with the studied parameters are presented in Table 4. The Cox regression analysis demonstrated an independent predictive value of renal venous congestion in relation to rehospitalization for DHF and achievement of the composite endpoint (Table 5).

Table 2

Comparative characteristics of patients with DHF with the absence and presence of renal venous congestion at admission

Parameter	Patients without renal venous congestion, *n* = 34	Patients with renal venous congestion, *n* = 90	*p*
LVEF < 40%, *n* (%) 41–49%, *n* (%) ≥ 50%, *n* (%)	 11 (32.4) 3 (8.8) 20 (58.8)	 37 (42.2) 20 (22.2) 32 (35.6)	0.045
Stagnation Scale, score, *Me [IQR]*	6 [4; 8]	11 [7; 13]	0.000
SPPA, mm Hg, *Me [IQR]*	34 [27; 40]	56 [40; 62]	<0.000
CKD in the medical history, *n* (%)	18 (52.9)	73 (81.1)	0.001
AKI, *n* (%)	2 (5.9)	27 (30)	0.004
Nt-proBNP, pg / ml, *Me [IQR]*	482.5 [339; 2,109]	1,699 [1,065; 3,131]	0.000
Creatinine, µmol / l, *Me [IQR]*	88 [74.7; 105]	109 [89; 134.6]	0.000
GFR, ml / min / 1.73m²	57.35 [50.8; 75]	53 [38; 61.9]	0.018
Urea, mmol / l, *Me [IQR]*	6.35 [4.72; 8.6]	7.66 [6.32; 10.5]	0.020
Uric acid, mmol / l, *Me [IQR]*	382.3 [285.1; 514.2]	501.63 [365.8; 587]	0.040
Potassium, mmol / l, *Me [IQR]*	4.2 [3.75; 4.55]	4.4 [4.05; 4.76]	0.027
Iron, mmol / l, *Me [IQR]*	10.86 [7.25; 15.17]	6.99 [5.32; 11.1]	0.023

Table 3

Characteristics of patients with DHF with changes in renal venous blood flow at discharge

Parameter	Persistence of continuous blood flow, *n* = 34	From discontinuous to continuous flow, *n* = 24	Persistence of discontinuous flow, *n* = 66	*p*
Gender, men, *n* (%)	14 (41.2)	15 (62.5)	35 (53)	0.26
Age, years, *Me [IQR]*	75.5 [68; 81]	67 [62.5; 72.5]	71.5 [64; 81]	0.125
Arterial hypertension, *n* (%)	31 (91.2)	23 (95.8)	56 (84.8)	0.300
Ischemic heart disease, *n* (%)	19 (55.9)	14 (58.3)	32 (48.5)	0.634
CKD, *n* (%)	18 (53)	21 (87.5)	52 (78.8)	0.004
AKI, *n* (%)	3 (8.8)	5 (20.8)	17 (25.8)	0.018
Atrial fibrillation, *n* (%)	18 (53)	13 (54.2)	42 (63.6)	0.513
Type 2 diabetes mellitus, *n* (%)	9 (26.5)	10 (41.7)	24 (36.6)	0.447
NYHA, FC, *n* (%) II III IV	 9 (26.5) 18 (52.9) 7 (20.6)	 7 (29.2) 11 (45.8) 6 (25)	 12 (18.2) 25 (37.8) 29 (44)	0.148
LVEF, %, *Me [IQR]*	52 [38; 58]	42 [33; 49]	44 [34; 55]	0.613
LVEF, *n* (%) < 40% 41–49% ≥ 50%	 11 (32.4) 3 (8.8) 20 (58.8)	 9 (37.5) 9 (37.5) 6 (25)	 28 (42.4) 11 (16.7) 27 (40.9)	0.017
NT-proBNP, pg / ml, *Me [IQR]*	482.5 [339; 2,109]	1,670.5 [905; 2,429]	1,700.5 [1,140; 3,412]	0.002
Creatinine, µmol / l, *Me [IQR]*	88 [74.7; 105]	108.5 [95.27; 130]	109 [87; 137]	0.001
GFR, ml / min / 1.73 m², *Me [IQR]*	57.35 [5-78; 75]	53.7 [45.57; 59.7]	53 [35.9; 66.7]	0.061
Blood potassium, mmol / l, *Me [IQR]*	4.2 [3.72; 4.55]	4.35 [4.05; 4.6]	4.41 [4.08; 4.77]	0.075
Urea, mmol / l, *Me [IQR]*	6.35 [4.72; 8.6]	7.45 [6.06; 9.9]	8.32 [6.56; 11.2]	0.053
Uric acid, mmol / l, *Me [IQR]*	382.3 [285.1; 514.2]	438.8 [399.3; 560]	505.4[357.15; 623.34]	0.107
Iron, mmol / l, *Me [IQR]*	10.86 [7.25; 11.78]	7.62 [5.8; 11]	6.77 [5.12; 11.2]	0.067

Table 4

Correlations of renal venous blood flow with laboratory and instrumental data in patients with DHF at admission and discharge

Parameter	On admission	At discharge
History of atrial fibrillation, *n* (%)	*p* = 0.007, *R* = 0.24	–
History of CKD	*p* = 0.000, *R* = 0.32	–
AKI, *n* (%)	*p* = 0.041, *R* = 0.25	–
Stagnation Scale, score	*p* = 0.000, *R* = 0.48	–
LVEF, *n* (%)	*p* = 0.021, *R* = –0.20	–
LVEF < 40% 41–49% > 50%	*p* = 0.017, *R* = –0.21	–
SPPA, mm Hg	*p* = 0.000, *R* = 0.50	–
Nt-proBNP, pg / ml	*p* = 0.000, *R* = 0.25	*p* = 0000, *R* = 0.30
Creatinine, μmol / l	*p* = 0.000, *R* = 0.34	*p* = 0.003, *R* = 0.25
GFR, ml / min / 1.73 m²	*p* = 0.020, *R* = –0.21	*p* = 0.018, *R* = –0.21
Iron, mmol / l	*p* = 0.012, *R* = –0.26	–
Uric acid, μmol / l	*p* = 0.024, *R* = 0.25	–
Potassium, mmol / l	*p* = 0.014, *R* = 0.22	–

Table 5

Cox regression analysis for renal venous congestion in terms of a risk of endpoint development

	Univariate regression analysis		Multivariate regression analysis	
	OR, 95% CI	*p*	OR, 95% CI	*p*
Rehospitalization for DHF	1.97 (1.03–3.75)	0.038	1.93 (1.017–3.67)	0.044
Composite endpoint	2.72 (1.46–5.06);	0.002	2.66 (1.43–4.96);	0.002

Note: OR – odds ratio, 95% CI – 95% confidence interval. The multivariate regression analysis included age, gender, LVEF < 40%, history of coronary artery disease, arterial hypertension, type 2 diabetes, CKD, and an increase in BMI a week prior to hospitalization.

Fig. 3 and Fig. 4 show the Kaplan – Meier curves for the cumulative survival probability (rehospitalizations and composite endpoints) depending on the presence of renal venous congestion.

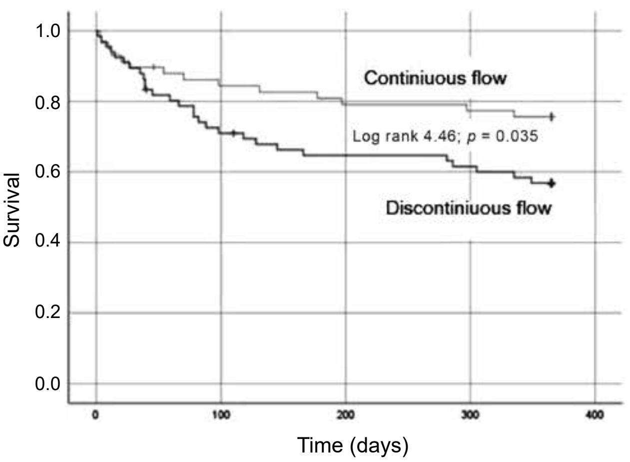

Fig. 3. Kaplan – Meier curves for cumulative survival probability (rehospitalizations) depending on the presence of renal venous congestion

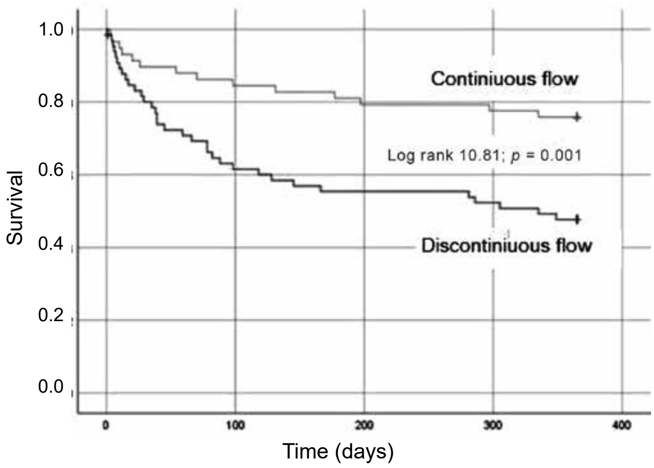

Fig. 4. Kaplan – Meier curves for cumulative survival probability (composite endpoints) depending on the presence of renal venous congestion

DISCUSSION

In our study, patients with DHF on admission were characterized by high incidence of venous renal congestion (in 72.6% of cases), assessed by Doppler ultrasound of the kidneys. Persistent renal venous congestion at discharge (in 53.2% of cases) was associated with the risk of one-year adverse outcomes. Our data are consistent with those of a recent study by A. Puzzovivo et al., who also found an association of venous renal congestion on ultrasound with the development of DHF and death during 36- month follow-up [7].

For many years, renal venous Doppler ultrasound has been used to assess non-cardiac conditions associated with elevated renal interstitial pressure, such as obstructive uropathy or diabetic nephropathy [8, 9]. However, recent data support the use of this imaging modality to assess intrarenal hemodynamics in HF [3, 4, 10].

A study by N. Iida et al., which examined the relationship of renal Doppler curves with the development of adverse outcomes among 224 patients with DHF, showed that discontinuous renal blood flow, including single-phase flow, had the most unfavorable prognosis (one-year survival < 40%) [3].

According to our results, renal venous congestion was associated with creatinine, GFR, uric acid, and potassium levels, development of AKI during hospitalization, and history of CKD. F. Husain-Syed et al. also found an association between renal venous congestion and worsening renal function in patients with HF [11].

The relationships revealed can be explained by the development mechanism of cardiac and renal dysfunction in HF, in which there is a decrease in cardiac output, an increase in intra-abdominal pressure, as well as an increase in venous pressure in the kidneys, leading to the occurrence of venous congestion, including renal one [12]. It is known that even minor renal damage in patients with HF is associated with high all-cause and cardiovascular mortality [13, 14].

CONCLUSION

In patients with DHF, the assessment of renal venous blood flow revealed high incidence of renal venous congestion and its prognostic value in the development of adverse outcomes, which makes it reasonable to use this technique in this group of patients.

Limitations and prospects of the study. The limitations of the study are associated with a small sample size and a relatively short follow-up period of 12 months.

There is an obvious need for a multicenter clinical study to investigate the nature of renal venous blood flow and its impact on the development of cardiovascular complications in patients with DHF.

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